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Anthropometry and plasma valine, amino acids, and proteins in the nutritional assessment of hemodialysis patients

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Anthropometry and plasma valine, amino acids, and proteins in the nutritional assessment of hemodialysis patients. Non-fasting plasma amino acids, proteins, anthropometric measurements, urea, and creatinine for 17 hemodialysis patients were compared with values in normal patients of similar age and sex. Values were characteristic for renal failure but with similarities to protein-energy malnutrition. Partial correlation coefficients, correcting for age and height, identified nutritional and non-nutritional factors. Plasma valine was the most correlated variable and was used to rank and group the patients. The group with valine less than 150 μm/liter had low values for 17 variables. Valine, isoleucine, leucine, threonine, asparagine, weight, and arm muscle circumference were interrelated and reflected malnutrition whereas fat correlated with calorie intake, and histidine and serine with protein intake. Taurine, aspartic acid, cystine, citrulline, urea, creatinine, prealbumin, and retinol-binding protein were decreased in malnutrition but were higher than normal due to a loss of renal function. Fourteen variables, less affected by malnutrition, were changed by specific non-nutritional factors. Hemodialysis patients of long standing (1 to 11 years), apart from two patients with recurrent sepsis, were adequately nourished, but those on hemodialysis for less than 15 months, most of whom had previously received peritoneal dialysis, were malnourished. Malnutrition in dialysis patients was due to protein and energy deficiency enhanced by metabolic abnormalities of amino acids. Our study shows that plasma valine is interrelated with other nutritional variables and may be used to assess protein-energy malnutrition.

Anthropométrie et partir de la valine, des acides aminés, et des proteins plasmatiques dans l'evaluation nutritionnelle des malades en hémodialyse. Les concentrations plasmatiques d'acides aminés et de protéines mesurées en dehors du jeûne, les mesures anthropométriques, l'urée et la créatinine de 17 malades en hémodialyse ont été comparées avec les valeurs obtenues chez des sujets normaux de même âge et de même sexe. Les valeurs étaient caractéristiques de l'insuffisance rénale mais avec des similitudes avec la malnutrition en protéines. Les coefficients de corrélation partielle qui ont permis la correction pour l'âge et la taille ont identifié des facteurs nutritionnels et non nutritionnels. La valine plasmatique est la variable la plus corrélée et a été utilisée pour classer et grouper les malades. Le groupe dont la valine est inférieure à 150 μm/litre avait des valeurs basses pour 17 variables. La valine, l'isoleucine, la leucine, la thréonine, l'asparagine, le poids et la circonférence du bras muscle étaient liés et reflétaient la malnutrition alors que la graisse était corrélée avec l'apport calorique et l'histidine et la sérine avec l'ingestion protéique. La taurine, l'acide aspartique, la cystine, la citrulline, l'urée, la créatinine, la préalbumine, la protéine liant le rétinol étaient diminués dans la malnutrition mais étaient supérieurs aux valeurs normales du fait de la perte de la fonction rénale. Quatorze variables, moins affectées par la malnutrition, étaient modifiées par des facteurs spécifiques non nutritionnels. Les malades en hémodialyse depuis un temps long (1 à 11 ans) mis à part deux d'entre eux qui avaient des septicémies récidivantes, étaient nourris de façon adéquate mais ceux qui étaient en hémodialyse depuis moins de quinze mois, dont la plupart avaient antérieurement été traités par dialyse péritonéale, étaient en situation de malnutrition. La malnutrition chez les malades en dialyse était due à un déficit en protéines et en énergie, augmenté par des anomalies du métabolisme des acide aminés. Cette étude montre que la valine plasmatique est liée à d'autres variables nutritionnelles et peut être utilisée pour évaluer la malnutrition en protéines et en énergie.

Morbidity and mortality in chronic renal failure frequently are associated with the long-term effects of conservative dietary treatment and intermittent hemodialysis. Many studies have shown that patients may develop protein-energy malnutrition if dietary protein and calories are insufficient to compensate for losses of amino acids and glucose in dialysis fluid [1–5], increased catabolism due to infection or other complications, blood loss and abnormalities of protein and amino acid metabolism. Frequently, the earliest indications of nutritional problems are low concentrations of plasma essential amino acids and plasma proteins such as transferrin [6–8]. In the long term, frank wasting may occur with an increased incidence of infections and clinical complications [4]. Recently, there have been several studies of patients with chronic renal failure in which biochemical and anthropometric measurements have been used to assess protein energy malnutrition [9–11]. However, there have been few attempts to assess the relative value of these variables in the detection of protein-energy malnutrition in chronic renal failure under controlled conditions. In our study we have compared a large number of variables, and from their interrelationships, we have evaluated the effects of dietary and other factors.

Methods

Seventeen non-fasted patients, twelve males and five females, ages 17 to 56 years and all receiving intermittent hemodialysis (HD), were each studied immediately before a routine dialysis. Each had been dialysed using dextrose free dialysis fluid over periods of 1 month to 11 years (mean equals 2 years, 7 months) with a 1.0 or 1.5 m^2 Kiil dialyser for 5 hours, three times a week, except for one patient for whom twice weekly was adequate. Most of the patients were allowed an

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unrestricted intake of protein and calories; this intake was assessed by the dietitian over a period of several months by regular interviews.

The mean daily intake was 72 g protein and 2,300 kcals although these intakes were probably overestimates as most patients ate less on dialysis days. Vitamin supplements and aluminum hydroxide were given daily. Thirteen patients were receiving hypotensive agents, and thirteen patients were receiving iron supplements. Each individual was examined and weighed. Blood was taken for analysis immediately before dialysis. Because six patients were dialysed in the morning, five in the afternoon, and six at night, the samples had to be non-fasting. Plasma was stored at −70° C before analysis. Normal values were obtained from members of the hospital staff who were matched for sex and age with the patients. The controls were in good health and consuming their usual diet. Their protein and caloric intakes were not assessed and were assumed to be adequate. Biceps, triceps, and subscapular skinfolds were measured and fat was calculated [12]. Arm muscle circumference (AMC) was derived from arm circumference (AC) and triceps skinfold (TSF), where AMC = AC − π (TSF). Plasma amino acids were measured using a Technicon T.S.M. amino acid analyser with a two-column procedure operating at 42° C and 61.5° C, respectively. Lithium citrate buffers were used for column elution, a complete analysis taking 6 hours. A Kemtronix 'Supergrator 3' was employed for quantitation using 50 μmoles of norleucine as an internal standard. Good separation was achieved for all the peaks measured and reproducibility was within ± 5% for most amino acids. Analyses were performed on 0.2 ml samples of heparinised plasma deproteinized by the addition of solid sulphosalicylic acid to a concentration of 5%. The concentration of tryptophan, glutamine, and glutamic acid are known to change both during storage and analysis and have not been included in the results. Plasma proteins were measured by radial immunodiffusion as described elsewhere [13].

Student's *t* test was used according to variance equivalence. The matrix of partial correlation coefficients, correcting for age and height, and ranked data were obtained from S.P.S.S. statistical programmes on an I.C.L. 1906A computer.

Results

Comparison between patients and normal individuals. Mean values for age, height, weight, fat, AMC, plasma protein fractions, hemoglobin, urea, and creatinine in the 17 patients immediately before a hemodialysis are compared with the age-matched control group in Table 1. The two groups were of similar mean age and height, and no significant differences were observed for weight, AMC, total protein, or albumin. However, the patients had lower values than controls for fat, transferrin, complement C3, and hemoglobin and higher values for prealbumin, retinol-binding protein (RBP), urea, and creatinine. Mean values for 16 plasma amino acids for the two groups are shown in Table 2. Valine, serine, tyrosine, histidine, and arginine were lower for patients than for controls but taurine, aspartic acid, glycine, alanine, citrulline, proline, ornithine, and cystine were higher. Isoleucine, leucine, and threonine (Table 2) and also those amino acids not shown in Table 2, that is, asparagine, methionine, phenylalanine, and lysine were at similar mean concentrations in both groups although many values were lower for individual patients. These observations are characteristic of dialysis patients with some degree of malnutrition as found in previous studies [4–8, 10, 11, 14, 15]. Our data were further analyzed to assess the contribution of both nutritional and non-nutritional factors.

Table 1. Mean values for age, anthropometric measurements, hemoglobin, and plasma proteins, urea and creatinine measurements in 17 patients on intermittent hemodialysis compared with 17 aged-matched normal individuals[a, d]

	Normal		Patients	
	Mean	SD	Mean	SD
Age *yr*	37.8	13.2	37.1	13.0
Height *cm*	171	8.1	169	9.5
Weight *kg*	67.5	6.4	63.6	12.1
Fat *kg*	18.0 (16)	4.5	13.1 (16)	5.5[b]
AMC *cm*	23.6 (16)	2.0	22.9 (16)	3.6
Transferrin *mg/100 ml*	297	45	224	41[c]
Hemoglobin *g/100 ml*	14.7	1.2	8.2	2.1[c]
Total protein *g/liter*	73 (16)	3.0	71 (16)	3.9
Albumin *g/liter*	42 (16)	1.4	41 (16)	3.1
Prealbumin *mg/100 ml*	33	3.3	42	12[e]
RBP *mg/100 ml*	6.2	1.7	24.8	6.2[f]
Complement C3 *mg/100 ml*	113	16	82	14[c]
Urea *mmoles/liter*	5.2	0.9	24.5 (16)	7.9[f]
Creatinine *moles/liter*	109	14	1042 (16)	235[f]

[a] Mean values significantly lower than normal; [b] $P < 0.01$; [c] $P < 0.001$.

[d] Mean values significantly higher than normal; [e] $P < 0.01$; [f] $P < 0.001$.

The number in parentheses refers to the number of patients or normal subjects other than 17. Abbreviations used are defined: AMC, arm muscle circumference; RBP, retinol-binding protein.

Effects of age, height, and sex. Pearson correlation coefficients, calculated for all the variables measured in patients and controls, showed that in both groups weight, AMC, and several amino acids were height-dependent and fat was age dependent. Consequently, partial correlation coefficients that statistically eliminated the effects of both height and age were calculated [16]. We did not differentiate between males and females because of the limited number of patients, however, data for the 12 males alone were generally similar to the whole group.

Partial correlation coefficients. A matrix of partial correlation coefficients, corrected for age and height in 17 patients and 17 controls, is shown for the most correlated variables in Figure 1. All these variables other than urea and creatinine have been used in previous studies to assess protein energy malnutrition [17].

(1) Controls. Branched chain amino acids, that is, valine, isoleucine, and leucine were highly interrelated ($P < 0.001$) probably because of their mutual dependence on dietary protein intake and the catabolism of muscle protein, and their degradation, principally in muscle, by a single transaminase. The other variables were generally unrelated with the exception of urea with proline and taurine ($P < 0.001$).

Table 2. Mean values for 16 plasma amino acids in 17 patients on intermittent hemodialysis compared with 17 age-matched normal individuals[a, d]

	Normal		Patients	
μmoles/liter	Mean	SD	Mean	SD
Valine	236	42	171	53[c]
Isoleucine	74	13	74	19
Leucine	140	27	122	44
Serine	118	24	82	25[c]
Tyrosine	66	11	41	16[c]
Histidine	117	15	100	32[b]
Arginine	109	20	91 (11)	21[b]
Threonine	137	25	132	49
Taurine	19	5	87	31[f]
Aspartic acid	16	5	44	14[f]
Glycine	216	38	340	115[f]
Alanine	444	47	570	169[e]
Citrulline	31	8	85	30[f]
Proline	144	28	258	90[f]
Ornithine	68	19	100 (14)	35[e]
Cystine	111	41	190	79[f]

[a] Mean values significantly lower than normal; [b] $P < 0.05$; [c] $P < 0.001$.

[d] Mean values significantly higher than normal; [e] $P < 0.01$; [f] $P < 0.001$.

The number in parentheses designates the number of patients or normal subjects other than 17.

	Wt	Fat	AMC	Val	Ile	Leu	Thr	Asn	Cre	Urea	P.I.	C.I.
Weight		** .77	** .68		* .62	* .64		* .61	** .75			
Fat									* .60			** .76
AMC				** .66	** .68	** .73		* .58	** .70	** .66		
Valine					*** 86	*** 95	*** 86	*** 81		** 76		
Isoleucine						*** .88	** .73	** .75	** .69	* .62		
Leucine							*** .81	*** .82		** .67		
Threonine								** .78		** .73		
Asparagine									* .64	** .72		
Creatinine												
Urea												
Protein intake												*** .76
Calorie intake												

Fig. 1. *Matrix of partial correlation coefficients, controlling for age and height in 17 patients for 12 variables.* One *asterisk* indicates $P < 0.05$; two, $P < 0.01$; and three, $P < 0.001$.

(2) Patients. Branched chain amino acids, particularly valine, were highly interrelated ($P < 0.001$) but also correlated with weight, AMC, urea, threonine, and asparagine (Fig. 2) and also citrulline ($P < 0.01$). AMC was the most highly correlated anthropometric measurement notably with weight, valine, isoleucine, leucine, asparagine, creatinine, and urea (Fig. 1) and also with albumin ($P < 0.01$), prealbumin, RBP, and taurine (all $P < 0.05$). Body fat correlated with weight, caloric intake ($P < 0.01$), creatinine, and serine ($P < 0.05$). Plasma proteins are not shown in Figure 1 as they were generally unrelated to one another (except transferrin with RBP, $P < 0.05$), amino acids or to anthropometric measurements (except AMC as previously shown). Plasma urea correlated with AMC, valine, isoleucine, leucine, threonine, and asparagine (Fig. 1) and also with tyrosine, phenylalanine, taurine, and RBP ($P < 0.01$), whereas creatinine correlated with weight, AMC with isoleucine ($P < 0.01$), asparagine and fat ($P < 0.05$). Dietary protein intake correlated with caloric intake ($P < 0.001$), plasma serine ($r = 0.67$; $P < 0.01$), and histidine ($r = 0.59$; $P < 0.05$). Several correlations were observed, when no correction was made for age and height, between dietary intake and body composition. Notably, protein intake (PI) versus weight ($r = 0.53$; $P < 0.05$); PI versus fat ($r = 0.79$; $P < 0.001$) PI versus AMC ($r = 0.54$; $P < 0.01$) and caloric intake (CI) versus weight ($r = 0.66$; $P < 0.01$). These relationships are similar to those in a comparable study [9] and can be attributed to effects of age and height, and they are not observed for corrected partial correlation coefficients. However, caloric intake correlated with body fat independently of height and age ($r = 0.64$; $P < 0.01$).

(3) Conclusions from the correlation data. With the exception of branched chain amino acids, correlations occurred within the patients but not for the control group. Valine and AMC were respectively the most correlated variables for the amino acids and anthropometric measurements while plasma proteins were only weakly correlated with a few variables. These interrelationships suggest a mutual dependence on several factors other than height or age. We believe that protein energy malnutrition is the most important factor.

Ranking by valine. The 17 patients were ranked by plasma valine because this amino acid was significantly lower than for normals (Table 2), was highly correlated with many of the variables (Fig. 1), and previously has been shown to reflect malnutrition [17]. The patients were divided into two groups, above or below 150 μmoles/liter of valine (2 SD below normal); the other corresponding values are shown in Table 3. The group of eight patients with lowest values for valine also had low values for 17 other variables. Six of these, valine, isoleucine, leucine, threonine, asparagine, weight, and AMC were interrelated as previously shown and closely reflect protein-energy malnutrition, whereas body fat correlated with caloric intake, and histidine and serine correlated with protein intake. The remaining variables that were decreased in the low valine group of patients (that is, taurine, aspartic acid, cystine, citrulline, urea, creatinine, prealbumin, and RBP) were nonetheless higher than normal (Table 2) due to loss of renal function or uremia.

Fourteen variables ranked against valine were not significantly lower in the malnourished group, and four of these are shown in Table 2. It is therefore likely that serine, tyrosine, arginine, transferrin, complement C3, and hemoglobin were all lower than normal mainly due to non-nutritional factors (Tables 1 and 2). However, the lowest values for these variables were found in the malnourished group. The gluconeogenic amino acids glycine, alanine, proline, and ornithine were unaffected by malnutrition and were higher than normal due to loss of renal function or uremia.

The ranked valine concentrations and corresponding values for leucine, threonine, urea, weight, fat, AMC, transferrin, prealbumin, asparagine, glycine, and creatinine are shown in Figure 2. These reflect the correlation data and show the

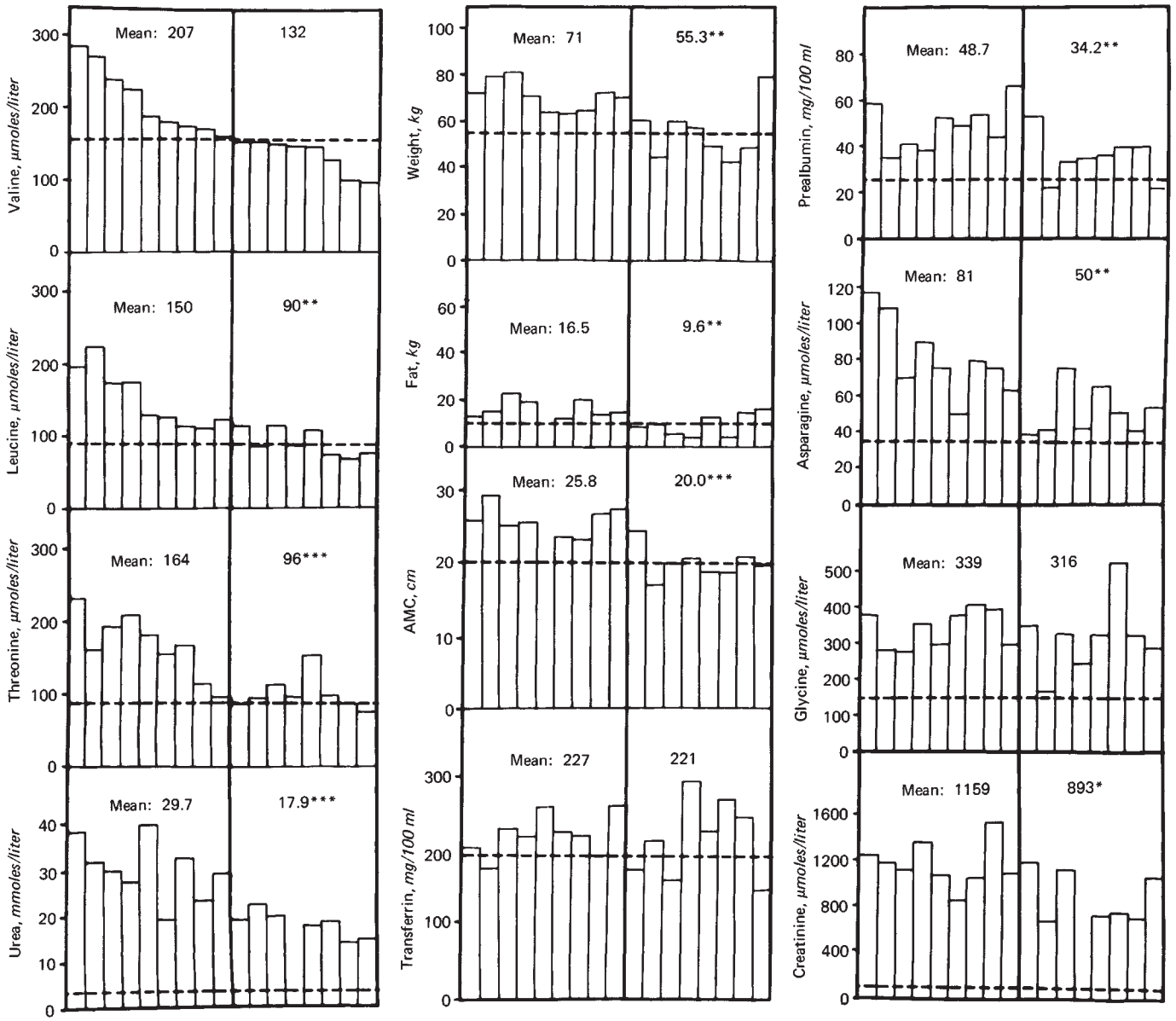

Fig. 2. *Patients ranked for plasma valine and the corresponding values for leucine, threonine, urea, weight, fat, AMC, transferrin, prealbumin, asparagine, glycine, and creatinine.* Mean values for each group with valine above or below 150 μmoles/liter are indicated. One *asterisk* indicates $P < 0.05$; two, $P < 0.01$; and three, $P < 0.001$. The *broken lines* represent 2 SD below the normal values.

relationship between some amino acids, anthropometric measurements, urea, and creatinine. In contrast, plasma transferrin and glycine were affected by non-nutritional factors.

Effects of dietary intake. Assessments of protein-energy malnutrition from plasma components should, ideally, be made at similar times of day to obviate diurnal variation, and by using fasting samples, minimize effects of preceding food intake [17]. Patients in this study were dialysed during a morning, afternoon, or evening schedule, and they were allowed their normal meals because it was impractical to fast all of them for comparable periods. Consequently, plasma valine and other amino acids were above fasting concentrations. However, food intake was depressed generally on dialysis days and was similar in quality and quantity for most patients. Blood was collected at similar time intervals after meals (90 ± 30 min) both in patients and controls. Differences in amino acid concentrations were not attributable to diurnal variation as patients sampled at different times of day were noted to be evenly distributed between the high and low valine groups. Valine concentrations were not increased disproportionately due to preceding meals, and they correlated with anthropometric variables which are unaffected by short-term effects. Furthermore, valine concentrations were lower for patients than for matched normals, lower than for fasted malnourished patients in a previous study [17], and they were not correlated with either protein or caloric intake. Most variables, including amino acids and urea, correlated predominantly with body composition and not with dietary intake. This correlation occurred probably because protein intake was lower

Table 3. Mean values for 24 variables in patients receiving intermittent hemodialysis grouped by valine concentration

	Ranking by valine concentration			
	Above 150 (9)[a]		Below 150 (8)[a]	
μmoles/liter	Mean	SD	Mean	SD
Valine	207	45.8	132	22.6
Isoleucine	85.7	17.6	59.9	8.9[b,d]
Leucine	150	40.1	90	18.3[d]
Threonine	164	42.7	96	24.1[e]
Histidine	116	24.9	81	30.7[c]
Taurine	112	17.6	59	13.2[e]
Aspartic acid	50.7	13.3	35.7	9.8[c]
Asparagine	81.0	21.3	50.6	13.3[d]
Cystine	234	86.4	142	21.6[d]
Citrulline	99.0	26.1	69	26.3[c]
Urea	29.7	6.4	17.9	2.9[e]
Creatinine	1159	177	893	223[c]
Weight *kg*	71	6.3	55.3	11.8[d]
Fat *kg*	16.5	3.9	9.6	4.6[d]
AMC *cm*	25.8	2.0	20.0	2.1[e]
Total protein *g/liter*	73.2	3.4	68.0	2.0[d]
Albumin *g/liter*	41.9	1.1	38.8	1.5
Transferrin *mg/100 ml*	227	28.3	221	53.7
Prealbumin *mg/100 ml*	48.7	10.4	34.2	9.0[d]
RBP *mg/100 ml*	27.6	6.2	21.7	4.8[c]
Complement C3 *mg/100 ml*	81.5	17.7	82.2	7.8
Hb *g/100 ml*	9.0	1.7	7.4	2.4
Protein intake *g/day*	83.7	26.5	57.7	13.6[c]
Caloric intake *kcal/day*	2558	548	1731	898[c]

[a] Number of patients.
[b] Mean values significantly different from the paired values; [c] $P < 0.05$; [d] $P < 0.01$; [e] $P < 0.001$. Abbreviations used are defined: AMC, arm muscle circumference; RBP, retinol-binding protein; Hb, hemoglobin.

for the malnourished group (Table 3), and the amino acids derived from this source were a small proportion of the total body pool. In contrast, plasma histidine and serine were low and were derived mainly from protein intake. Caloric intake was also lower for this group (Table 3) and was related to body fat. However, if daily intake is calculated per kg of body wt, both groups received similar intakes of protein (1.1 g/kg) and calories (36 kcal/kg). Clearly, this intake maintained an existing nutritional state but did not promote growth in the malnourished patients. A higher total intake should be calculated from the relative weight for normal individuals of the same age and height rather than from malnourished weight.

Effects of non-dietary factors. Several factors, other than dietary intake, that may have contributed to malnutrition or affected the values of the variables measured are shown in Table 4. None would cause sudden changes on the day of study: *(1) Sex.* Four of the five women were in the lower valine group (Table 4) which is compatible with the lower values expected for women. However, valine concentrations and other variables were generally lower for the female patients than for the matched female controls, and this suggests nutritional depletion due to factors unrelated to sex. Several other factors are shown in Table 4 and are considered for the whole group of patients. *(2) Dialysis.* The nine patients with valine greater than 150 μmoles/liter (Table 4) were maintained on HD for between 1 and 11 years and had never received intermittent peritoneal dialysis (PD). Of the eight patients in the malnourished group (valine less than 150 μmoles/liter), six had received HD for 1 to 5 months while two patients on HD for 2 and 6 years, respectively, had recurrent septicemia. Five of these malnourished patients had been treated by PD for periods of 1 to 6 months before HD was started. This finding suggests that PD may have caused nutritional depletion; this condition was not corrected during subsequent HD. *(3) Iron supplements.* Thirteen patients received daily Ferrograd C or ferrous sulphate. Plasma transferrin may be increased in iron deficiency and decreased during iron therapy [18]. *(4) Sepsis.* Three malnourished patients had recurrent infections: two with intermittent septicemia and one with respiratory infection. *(5) Plasma insulin.* Mean plasma insulin for malnourished patients was 15.2 μU/ml and was similar to the normal value of 14.9 μU/ml, whereas, for patients with normal valine, the concentration was significantly higher at 31.1 μU/ml ($P < 0.05$). This concentration suggests that the decrease of valine was not caused by hyperinsulinemia.

Discussion

Nutritional surveys and studies of surgical patients have shown that protein-energy malnutrition may be assessed from plasma amino acids [17, 19], proteins [13, 20], or anthropometric measurements [21, 22]. In our study we have compared these variables in patients receiving intermittent hemodialysis with the same variables for normal individuals of similar age and sex. Patients had markedly lower values for plasma valine, transferrin, and body fat, but other variables were low and many were interrelated independently of age and height. Plasma valine was most correlated and was used to rank and divide the patients into two groups; those with the lowest measurement of valine also had low values for seventeen other variables. We believe that this high incidence of low values can be attributed primarily to the net effect of protein-energy deficiency as was also found in a similar study of surgical patients [17]. However, several of the variables were either excessively low or above normal values due to a loss of renal function, uremia, or hemodialysis.

The branched chain amino acids valine, isoleucine, and leucine play a central role in metabolism as precursors for the synthesis of proteins, fatty acids, metabolic fuel, regulators of protein turnover, and insulin release [23]. The relationship between these three branched chain amino acids in the blood of controls and patients may be attributed to their mutual dependence on dietary protein intake, the catabolism of muscle protein, and also on their degradation, principally in muscle by a single transaminase. We have found previously that long-term protein-energy deficiency in surgical patients causes a decrease in plasma valine with a proportional reduction in many amino acids, proteins, and muscle mass [17]. Similar effects in dialysis patients were found in this study, but protein-energy malnutrition was enhanced by metabolic defects of amino acids. Plasma isoleucine and leucine were normal except in the malnourished patients whereas valine was decreased more than would be expected from malnutrition alone. Concentrations of valine were generally lower than in fasting patients with severe weight loss [17]. Previous studies have indicated that valine may be decreased in renal failure, both in plasma [24] and muscle [25] due to factors other than malnutrition. Alterations in muscle

Table 4. Sex, diagnosis, and details of treatment for the 17 patients ranked by plasma valine

Patient nos.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Valine *μmoles/liter*	281	266	236	221	183	178	171	167	157	149	149	146	145	144	126	98	96
Sex	M	M	M	M	M	M	F	M	M	M	F	M	M	F	F	F	M
Diagnosis	CGN	PCD	CGN	RHN	HRF	HRF	RHN	CGN	APN	RHN	HRF	AS	CGN	CPN	HRF	DIN	CN
Previous treatment	C	C	C	C	C	C	C	C	C	P	P	C	P	C	C	P	P
Time, *months*	—	—	—	—	—	—	—	—	—	1	3	—	2	—	—	6	2
Hemodialysis, *per week*	3	3	3	3	2	3	3	3	3	3	3	3	3	3	3	3	3
Time, *months*	40	36	135	87	16	20	18	32	12	24	1	4	12	2	1	16	78
Sepsis	—	—	—	—	—	—	—	—	—	S	PE	—	—	—	—	—	S/Ps

Abbreviations used are defined: CGN, chronic glomerulonephritis; PCD, polycystic disease; RHN, reflux hydronephrosis; HRF, hypertensive renal failure; APN, acute polyarteritis nodosa; AS, Alport syndrome; CPN, chronic pyelonephritis; DIN, drug induced nephropathy; CN, chronic nephritis; C, conservative therapy; P, intermittent peritoneal dialysis; S, recurrent septicemia; PE, pleural effusion; Ps, psoriasis.

uptake and release could be caused by increases in hormones such as insulin or parathormone [26], but in our study insulin concentration was normal for the malnourished patients. A deficiency of valine would be compatible with increased degradation. Decreased decarboxylation has been found in fasting uremic patients [24] although valine is not oxidized completely to carbon dioxide in skeletal muscle. In rat muscle more than 50% of valine and also isoleucine, asparagine, glutamic acid, and aspartic acid are converted to glutamine while a proportion of each is released unchanged into the circulation [27]. Glutamine may be metabolized to alanine in the kidney or intestine and then converted to glucose and urea in the liver. Enhanced degradation of valine via glutamine would be consistent with increased turnover of glucose and alanine in chronic renal failure [28]. This mechanism would aid the removal of ammonia from muscle and provide substrate for gluconeogenesis. In our study plasma asparagine and threonine concentrations were related to branched chain amino acids, and both were normal except in malnourished patients. Abnormal concentrations of several amino acids can be attributed to altered uptake and release by the diseased kidney [29]. Tyrosine, arginine, and serine were low in our dialysis patients probably due to reduced kidney release. Low tyrosine has been a constant finding in renal failure [4, 14, 30] and can be attributed to decreased hydroxylation in the kidneys and liver. Tyrosine release by the normal kidney, caused by low activity of phenylalanine hydroxylase relative to that in liver [31, 32], is decreased by renal impairment [29]. Decreased hydroxylation by the liver, due to severe malnutrition or uremia, may also decrease plasma tyrosine [31]. Impairment of renal function reduces the conversion of citrulline to arginine and glycine to serine [29]; consequently, plasma arginine and serine are reduced. The concentration of serine, like that of histidine, is dependent on the availability of dietary protein. Most of the amino acids that were increased in our patients were, like urea and creatinine, lowest in the malnourished group and were therefore, unlikely to have contributed to nutritional impairment. However, our data suggest that decrease in plasma amino acids, whether due specifically to a deficiency of protein and energy or to metabolic abnormality, is associated with a decrease in body proteins particularly in muscle and liver with eventual wasting.

The increased concentrations of prealbumin and retinol-binding protein in this and previous studies of chronic renal failure [15, 33, 34] emphasize the role of the healthy kidney in the degradation of low molecular weight proteins [35]. However, both proteins were at lowest concentrations in the malnourished patients, and they were weakly related to muscle (AMC) and several other variables, suggesting that they reflect the availability of nutrient supply. Optimal synthesis of both proteins is dependent on an adequate supply of glucose and amino acids [36, 37]. In contrast albumin, a higher molecular weight protein metabolized mainly in the liver and generally less sensitive to nutrition, was normal in all but three of the most malnourished patients. Transferrin, complement C3, and also hemoglobin were markedly lower than normal due mainly to renal disease. Previous studies have shown that transferrin is decreased in chronic renal failure and in patients receiving hemodialysis [30, 38, 39]. Concentrations are usually lowest in malnourished patients [7] and may be increased by supplementation with amino acids, proteins, and carbohydrates [8], although normal concentrations are not achieved [34]. Clearly such changes are unlikely in well-nourished patients or if transferrin is affected mainly by non-nutritional effects. Thus, concentration may be increased in iron deficiency or decreased by iron supplementation [18]. Iron supplementation probably contributed to the low plasma transferrin in our patients, particularly in those that were adequately nourished. However, impairment of renal function or uremia may decrease transferrin independently of nutrition [4, 38]. The metabolic abnormalities previously described may reduce the availability of amino acids in plasma for the synthesis of plasma proteins, and this state may not be corrected by supplementary food intake.

Normal individuals in this study were receiving an adequate diet and consequently plasma amino acids, proteins, and body composition were unrelated. In contrast these components were interrelated in dialysis patients receiving marginally adequate or deficient dietary protein and calories as was also found in surgical patients [17] and in rats with experimental chronic renal insufficiency [40]. These observations suggest that decreases in plasma amino acids, particularly valine, may be associated with a reduction in plasma protein synthesis in the liver, gradual loss of muscle, and a reduction in urea produc-

tion. These changes are characteristic of protein-energy malnutrition; in dialysis patients they can be attributed partly to loss of renal function, endocrine disorders, and dialysis in addition to nutritional inadequacy. Protein and energy intakes were adequate in nine of the patients, all of whom had been maintained on HD for periods of 1 to 11 years but was insufficient in the malnourished group, most of whom had been on HD for shorter periods. This suggests the protein-energy malnutrition was caused preceding HD and that protein intake during a period up to 1 year was insufficient to maintain plasma histidine or correct the deficiency in branched chain and other amino acids, or restore plasma and muscle proteins while caloric intake was insufficient to restore body fat A high proportion of these patients previously had received PD which frequently causes nutritional depletion [30]. Two had recurren septicemia and one had a respiratory infection thereby enhancing malnutrition. Clearly, a prolonged period of malnutrition caused by PD or excessive dietary restriction before HD should be avoided and patients actively encouraged to eat more protein (1.2 to 1.5 g/kg/day) and calories (35 to 45 kcal/kg/day) calculated from the relative weight for normal individuals of the same height and age rather than from malnourished weight.

We conclude that protein-energy malnutrition may occur in dialysis patients due to dietary inadequacy and also to metabolic abnormalities of amino acids. This progressive condition may be defined from concentrations of amino acids, plasma proteins, and anthropometric measurements. Importantly, plasma valine is interrelated with other nutritional variables and has a useful role in the assessment of protein-energy malnutrition. However, plasma amino acids and proteins are rapidly changed by stress, sepsis, or sudden alteration of the quantity or balance of protein and energy in the diet. Consequently, interpretation should be made on patients in a stable state, preferably fasting or compared with pair-matched controls [17].

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